Retevmo® (selpercatinib)

Treatment Plan Guide

INDICATIONS

Retevmo is a kinase inhibitor indicated for the treatment of:

- adult patients with metastatic *RET* fusion-positive non-small cell lung cancer (NSCLC)
- adult and pediatric patients 12 years of age and older with advanced or metastatic *RET*-mutant medullary thyroid cancer (MTC) who require systemic therapy
- adult and pediatric patients 12 years of age and older with advanced or metastatic *RET* fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate)

These indications are approved under accelerated approval based on overall response rate (ORR) and duration of response (DoR). Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

RET=rearranged during transfection.

Disclaimer: This guide is intended to provide information to develop a drug record for Retevmo and/or to assist users with creating a standard treatment template for use of Retevmo in the treatment of adult patients with metastatic *RET* fusion-positive NSCLC OR adult and pediatric patients 12 years of age and older with advanced or metastatic *RET*-mutant MTC who require systemic therapy OR adult and pediatric patients 12 years of age and older with advanced or metastatic *RET* fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate). Patients should be evaluated by a physician prior to the use of Retevmo and deemed to meet both a confirmatory diagnosis of any of the above indications and be an appropriate candidate for the use of Retevmo. Based on individual patient cases and unique scenarios, additional tests, assessments and medications may be necessary for the proper care and treatment of patients receiving this regimen. This guide does not constitute a final order and may not meet the comprehensive needs of individual patients or institutions.

IMPORTANT SAFETY INFORMATION FOR RETEVMO

Hepatotoxicity: Serious hepatic adverse reactions occurred in 2.6% of patients treated with Retevmo. Increased aspartate aminotransferase (AST) occurred in 51% of patients, including Grade 3 or 4 events in 8% and increased alanine aminotransferase (ALT) occurred in 45% of patients, including Grade 3 or 4 events in 9%. The median time to first onset for increased AST was 4.1 weeks (range: 5 days to 2 years) and increased ALT was 4.1 weeks (range: 6 days to 1.5 years). Monitor ALT and AST prior to initiating Retevmo, every 2 weeks during the first 3 months, then monthly thereafter and as clinically indicated. Withhold, reduce dose or permanently discontinue Retevmo based on the severity.

Hypertension occurred in 35% of patients, including Grade 3 hypertension in 17% and Grade 4 in one (0.1%) patient. Overall, 4.6% had their dose interrupted and 1.3% had their dose reduced for hypertension. Treatment-emergent hypertension was most commonly managed with anti-hypertension medications. Do not initiate Retevmo in patients with uncontrolled hypertension. Optimize blood pressure prior to initiating Retevmo. Monitor blood pressure after 1 week, at least monthly thereafter, and as clinically indicated. Initiate or adjust anti-hypertensive therapy as appropriate. Withhold, reduce dose, or permanently discontinue Retevmo based on the severity.

Please see Important Safety Information throughout and click for full Prescribing Information for Retevmo.

Lilly

Retevmo®
selpercatinib capsules
40 mg • 80 mg

Pharmacology[1]

Class	*RET* Kinase Inhibitor
Mechanism of Action	Kinase inhibitor of *RET* (and other kinases)

Treatment[1]

Category	Details
Regimen	Retevmo Days 1-30
FDA-Approved Indication	Retevmo is a kinase inhibitor indicated for the treatment of: • adult patients with metastatic *RET* fusion-positive non-small cell lung cancer (NSCLC) • adult and pediatric patients 12 years of age and older with advanced or metastatic *RET*-mutant medullary thyroid cancer (MTC) who require systemic therapy • adult and pediatric patients 12 years of age and older with advanced or metastatic *RET* fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate) These indications are approved under accelerated approval based on overall response rate and duration of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.
Patient Selection	Patient selection for treatment with Retevmo should be based on the presence of a *RET* gene fusion (NSCLC) or specific *RET* gene mutation (MTC) in tumor specimens or plasma*

Treatment Medication[1]

Dosing	**Recommended starting dose** The recommended dosage of Retevmo based on body weight is†: • <50 kg: 120 mg PO BID • ≥50 kg: 160 mg PO BID
Dosage forms and strength	Retevmo is available in bottles as 80-mg and 40-mg capsules dispensed in 30-day supplies based on BID oral administration

Treatment Schedule[1]

Treatment Days	Daily
Cycle Length	30 days
Treatment Duration	Continuously until disease progression or unacceptable toxicity

*An FDA-approved test for the detection of *RET* gene fusions and *RET* mutations is not currently available.
†Dose interruptions and/or dose reductions may be required based on individual safety and tolerability. Refer to the full Prescribing Information for more complete information.
BID=twice daily; PO=orally.

IMPORTANT SAFETY INFORMATION FOR RETEVMO (CONTINUED)

Retevmo can cause concentration-dependent **QT interval prolongation.** An increase in QTcF interval to >500 ms was measured in 6% of patients and an increase in the QTcF interval of at least 60 ms over baseline was measured in 15% of patients. Retevmo has not been studied in patients with clinically significant active cardiovascular disease or recent myocardial infarction. Monitor patients who are at significant risk of developing QTc prolongation, including patients with known long QT syndromes, clinically significant bradyarrhythmias, and severe or uncontrolled heart failure. Assess QT interval, electrolytes and TSH at baseline and periodically during treatment, adjusting frequency based upon risk factors including diarrhea. Correct hypokalemia, hypomagnesemia and hypocalcemia prior to initiating Retevmo and during treatment. Monitor the QT interval more frequently when Retevmo is concomitantly administered with strong and moderate CYP3A inhibitors or drugs known to prolong QTc interval. Withhold and dose reduce or permanently discontinue Retevmo based on the severity.

Please see Important Safety Information throughout and click for full Prescribing Information for Retevmo.

Monitoring[1]

Clinical Assessment	Laboratory and other clinical tests may be ordered more frequently at the discretion of the provider or according to institutional standards. • **Hepatotoxicity:** Monitor ALT and AST prior to initiating Retevmo, every 2 weeks during the first 3 months, then monthly thereafter and as clinically indicated • **Hypertension:** Monitor blood pressure after 1 week, at least monthly thereafter and as clinically indicated • **QT interval prolongation:** – Monitor patients who already have or who are at significant risk of developing QTc prolongation, including patients with known long QT syndromes, clinically significant bradyarrhythmias, and severe or uncontrolled heart failure. Assess QT interval, electrolytes and TSH at baseline and periodically during treatment, adjusting frequency based upon risk factors including diarrhea. Correct hypokalemia, hypomagnesemia and hypocalcemia prior to initiating Retevmo and during treatment – Monitor the QT interval more frequently when Retevmo is concomitantly administered with strong and moderate CYP3A inhibitors or drugs known to prolong QTc interval • **Assess patients for the following:** – **Hemorrhagic events** – **Hypersensitivity reactions** – **Tumor lysis syndrome** – **Risk of impaired wound healing** – **Embryo-fetal toxicity** • **Potential consideration:** Consider alternative markers of renal function if persistent elevations in serum creatinine are observed. Serum creatinine increased 18% after 10 days in healthy volunteers given Retevmo 160 mg BID
Treatment Parameters	Labs and clinical assessments should be monitored to evaluate treatment, toxicity and for dose modifications at the discretion of the treating provider. • **Hepatotoxicity:** Withhold, reduce dose, or permanently discontinue Retevmo based on the severity of ALT/AST increase • **Hypertension:** Optimize blood pressure prior to initiating Retevmo. Monitor blood pressure after 1 week, at least monthly thereafter and as clinically indicated. Initiate or adjust anti-hypertensive therapy as appropriate. Withhold, reduce dose, or permanently discontinue Retevmo based on the severity • **QT interval prolongation:** Withhold and dose reduce or permanently discontinue Retevmo based on the severity • **Hemorrhagic events:** Permanently discontinue Retevmo in patients with severe or life-threatening hemorrhage • **Hypersensitivity:** If hypersensitivity occurs, withhold Retevmo and begin corticosteroids at a dose of 1 mg/kg prednisone (or equivalent). Upon resolution of the event, resume Retevmo at a reduced dose and increase the dose of Retevmo by 1 dose level each week as tolerated until reaching the dose taken prior to onset of hypersensitivity. Continue steroids until patient reaches target dose and then taper. Permanently discontinue Retevmo for recurrent hypersensitivity • **Tumor lysis syndrome (TLS):** Patients may be at risk of TLS if they have rapidly growing tumors, a high tumor burden, renal dysfunction, or dehydration. Closely monitor patients at risk, consider appropriate prophylaxis including hydration, and treat as clinically indicated. • **Risk of impaired wound healing:** Withhold Retevmo for at least 7 days prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of Retevmo after resolution of wound healing complications has not been established • **Embryo-fetal toxicity:** Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with Retevmo and for at least 1 week after the final dose

Administration Considerations[1]

Administration	• The recommended dosage of Retevmo based on body weight is: – <50 kg: 120 mg – ≥50 kg: 160 mg • Take Retevmo PO BID approximately every 12 hours until disease progression or until unacceptable toxicity • Swallow the capsules whole. Do not crush or chew the capsules • Do not take a missed dose unless it is more than 6 hours until next scheduled dose. If vomiting occurs after Retevmo administration, do not take an additional dose, and continue to the next scheduled time for the next dose
Food Interactions	• Retevmo may be taken with or without food • If coadministered with a proton pump inhibitor (PPI), take Retevmo with food
Dose Modifications	• Retevmo dose should be modified for hepatotoxicity, hypertension, QT interval prolongation, hemorrhagic events, hypersensitivity reactions, and other adverse reactions (ARs) • Retevmo dose should be modified for concomitant use of acid-reducing agents, strong and moderate CYP3A inhibitors, and severe hepatic impairment

ALT=alanine transaminase; AST=aspartate aminotransferase; CYP3A4=cytochrome P450 3A4.

Retevmo®
selpercatinib capsules
40 mg • 80 mg

How Supplied[1]

Capsule Strength	Quantity of Capsules per Bottle	NDC	Days' Supply
80 mg	120 count	0002-2980-26	**30 days (based on BID administration)**
80 mg	60 count	0002-2980-60	
40 mg	60 count	0002-3977-60	

Capsule Strength and Dosing Regimen: 30-Day Supply[1]

Target Dose	Dosage Modification: Patient Weight ≥50 kg	Dosage Modification: Patient Weight <50 kg	How Dispensed	Required Quantity of 80-mg 120-count bottles	Required Quantity of 80-mg 60-count bottles	Required Quantity of 40-mg 60-count bottles
160 mg PO BID	Standard Dose	–	Two (2) 80-mg capsules BID	1	0	0
120 mg PO BID	First Dose Reduction	Standard Dose	Three (3) 40-mg capsules BID	0	0	3
80 mg PO BID	Second Dose Reduction	First Dose Reduction	One (1) 80-mg capsule BID	0	1	0
40 mg PO BID	Third Dose Reduction	Second Dose Reduction	One (1) 40-mg capsule BID	0	0	1
40 mg PO QD	–	Third Dose Reduction	One (1) 40-mg capsule QD	0	0	1*

*For 40-mg capsule QD dosing, dispensing a 40-mg 60-count bottle will provide a 60-day supply.
NDC=National Drug Code; QD=daily.

IMPORTANT SAFETY INFORMATION FOR RETEVMO (CONTINUED)

Serious, including fatal, **hemorrhagic events** can occur with Retevmo. Grade ≥3 hemorrhagic events occurred in 2.3% of patients treated with Retevmo including 3 (0.4%) patients with fatal hemorrhagic events, including one case each of cerebral hemorrhage, tracheostomy site hemorrhage, and hemoptysis. Permanently discontinue Retevmo in patients with severe or life-threatening hemorrhage.

Hypersensitivity occurred in 4.3% of patients receiving Retevmo, including Grade 3 hypersensitivity in 1.6%. The median time to onset was 1.7 weeks (range 6 days to 1.5 years). Signs and symptoms of hypersensitivity included fever, rash and arthralgias or myalgias with concurrent decreased platelets or transaminitis. If hypersensitivity occurs, withhold Retevmo and begin corticosteroids at a dose of 1 mg/kg prednisone (or equivalent). Upon resolution of the event, resume Retevmo at a reduced dose and increase the dose of Retevmo by 1 dose level each week as tolerated until reaching the dose taken prior to onset of hypersensitivity. Continue steroids until patient reaches target dose and then taper. Permanently discontinue Retevmo for recurrent hypersensitivity.

Please see Important Safety Information throughout and click for full Prescribing Information for Retevmo.

Dose Modifications/Reductions for ARs and Concomitant Use of Select Therapies[1]

Adverse Reaction	Dosage Modification
Hepatotoxicity (Grade 3 or 4)	• Withhold Retevmo and monitor AST/ALT once weekly until resolution to Grade 1 or to baseline • Resume at a reduced dose by 2 dose levels and monitor AST and ALT once weekly until 4 weeks after reaching dose taken prior to the onset of Grade 3 or 4 increased AST or ALT • Increase dose by 1 dose level after a minimum of 2 weeks without recurrence and then increase to dose taken prior to the onset of Grade 3 or 4 increased AST or ALT after a minimum of 4 weeks without recurrence
Hypertension (Grade 3)	• Withhold Retevmo for Grade 3 hypertension that persists despite optimal antihypertensive therapy • Resume at a reduced dose when hypertension is controlled
Hypertension (Grade 4)	• Discontinue Retevmo
QT Interval Prolongation (Grade 3)	• Withhold Retevmo until recovery to baseline or Grade 0 or 1 • Resume at a reduced dose
QT Interval Prolongation (Grade 4)	• Discontinue Retevmo
Hemorrhagic Events (Grade 3 or 4)	• Withhold Retevmo until recovery to baseline or Grade 0 or 1 • Discontinue Retevmo for severe or life-threatening hemorrhagic events
Hypersensitivity Reactions (All Grades)	• Withhold Retevmo until resolution of the event. Initiate corticosteroids • Resume at a reduced dose by 3 dose levels while continuing corticosteroids • Increase dose by 1 dose level each week until the dose taken prior to the onset of hypersensitivity is reached, then taper corticosteroids
Other Adverse Reactions Grade 3 or 4)	• Withhold Retevmo until recovery to baseline or Grade 0 or 1 • Resume at a reduced dose

Dose Management for Concomitant Use		
Strong and Moderate CYP3A Inhibitors	• Avoid concomitant use of strong and moderate CYP3A inhibitors with Retevmo • If concomitant use of strong and moderate CYP3A inhibitors cannot be avoided, reduce the Retevmo dosage	• If concomitant use of strong CYP3A inhibitors cannot be avoided, reduce Retevmo dose from 160 mg and 120 mg BID to 80 mg and 40 mg BID, respectively • If concomitant use of moderate CYP3A inhibitors cannot be avoided, reduce Retevmo dose from 160 mg and 120 mg BID to 120 mg and 80 mg BID, respectively
Acid-Reducing Agents	• Avoid concomitant use of PPI, a histamine-2 (H2) receptor antagonist, or a locally-acting antacid with Retevmo	• If concomitant use cannot be avoided: – Take Retevmo with food when coadministered with a PPI – Take Retevmo 2 hours before or 10 hours after administration of an H2 receptor antagonist – Take Retevmo 2 hours before or 2 hours after administration of a locally-acting antacid

Reduce the recommended dosage of Retevmo for patients with severe hepatic impairment to 80 mg PO BID.

Retevmo®
selpercatinib capsules
40 mg • 80 mg

Storage and Handling[1]

Strength[1]	80-mg and 40-mg capsules
Hazardous classification[2]	• **Physical hazards:** not classified • **Health hazards:** reproductive toxicity (category 1B); specific target organ toxicity, single exposure (category 2); specific target organ toxicity, repeated exposure (category 2); germ cell mutagenicity (category 2) • **OSHA defined hazards:** combustible dust
Hazard statement[2]	May form combustible concentrations in air H341: Suspected of causing genetic defects H360: May damage fertility or the unborn child H371: May cause damage to organs (bone marrow) H373: May cause damage to organs (gastrointestinal tract) through prolonged or repeated exposure
Storage	Keep Retevmo capsules at room temperature between 20°C to 25°C (68°F to 77°F); temperature excursions between 15°C and 30°C (59°F to 86°F) are permitted.[1] Keep container tightly closed in a dry and well-ventilated place.[2]
Precautions for safe handling[2]	Avoid contact with eyes, skin, and clothing
Disposal[2]	Dispose of contents/container in accordance with local/regional/national/international regulations
Stability and reactivity[2]	• Reactivity: not water reactive • Chemical stability: material is stable under normal conditions • Possibility of hazardous reactions: hazardous polymerization does not occur

OSHA=Occupational Safety and Health Administration.

IMPORTANT SAFETY INFORMATION FOR RETEVMO (CONTINUED)

Tumor lysis syndrome (TLS) occurred in 1% of patients with medullary thyroid carcinoma receiving Retevmo. Patients may be at risk of TLS if they have rapidly growing tumors, a high tumor burden, renal dysfunction, or dehydration. Closely monitor patients at risk, consider appropriate prophylaxis including hydration, and treat as clinically indicated.

Impaired wound healing can occur in patients who receive drugs that inhibit the vascular endothelial growth factor (VEGF) signaling pathway. Therefore, Retevmo has the potential to adversely affect wound healing. Withhold Retevmo for at least 7 days prior to elective surgery. Do not administer for at least 2 weeks following major surgery and until adequate wound healing. The safety of resumption of Retevmo after resolution of wound healing complications has not been established.

Based on data from animal reproduction studies and its mechanism of action, Retevmo can cause **fetal harm** when administered to a pregnant woman. Administration of selpercatinib to pregnant rats during organogenesis at maternal exposures that were approximately equal to those observed at the recommended human dose of 160 mg twice daily resulted in embryolethality and malformations. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with Retevmo and for at least 1 week after the final dose. There are no data on the presence of selpercatinib or its metabolites in human milk or on their effects on the breastfed child or on milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with Retevmo and for 1 week after the final dose.

Please see Important Safety Information throughout and click for full Prescribing Information for Retevmo.

Patient Counseling[1]

Administration	• The recommended dosage of Retevmo is based on body weight: – <50 kg: 120 mg PO BID – ≥50 kg: 160 mg PO BID • Take Retevmo PO BID (approximately every 12 hours) until disease progression or unacceptable toxicity[1] • Retevmo may be taken with or without food • If coadministered with a proton pump inhibitor (PPI), take Retevmo with food • Swallow the capsules whole. Do not crush or chew the capsules • Do not take a missed dose unless it is more than 6 hours until next scheduled dose. If vomiting occurs after Retevmo administration, do not administer an additional dose, and continue to the next scheduled time for the next dose
Drug Interactions*	• **Acid-Reducing Agents:** Avoid concomitant use of PPIs, H2 receptor antagonists, and locally-acting antacids with Retevmo. If coadministration cannot be avoided, take Retevmo with food (with a PPI) or modify its administration time (with a H2 receptor antagonist or a locally-acting antacid) • **Strong and Moderate CYP3A4 inhibitors:** Avoid concomitant use of strong and moderate CYP3A inhibitors with Retevmo. If concomitant use of strong and moderate CYP3A inhibitors cannot be avoided, reduce the Retevmo dosage and monitor the QT interval with ECGs more frequently • **Strong and Moderate CYP3A4 inducers:** Avoid coadministration of strong or moderate CYP3A4 inducers with Retevmo • **CYP2C8 and CYP3A substrates:** Avoid coadministration of Retevmo with CYP2C8 and CYP3A substrates where minimal concentration changes may lead to increased adverse reactions. If coadministration cannot be avoided, follow recommendations for CYP2C8 and CYP3A substrates provided in their approved product labeling
Adverse Reactions and Laboratory Abnormalities	• The most common adverse reactions, including laboratory abnormalities, (≥25%) were increased aspartate aminotransferase (AST), increased alanine aminotransferase (ALT), increased glucose, decreased leukocytes, decreased albumin, decreased calcium, dry mouth, diarrhea, increased creatinine, increased alkaline phosphatase, hypertension, fatigue, edema, decreased platelets, increased total cholesterol, rash, decreased sodium, and constipation • Serious adverse reactions occurred in 33% of patients who received Retevmo. The most frequent serious adverse reaction (in ≥2% of patients) was pneumonia. Fatal adverse reactions occurred in 3% of patients; fatal adverse reactions which occurred in >1 patient included sepsis (n=3), cardiac arrest (n=3) and respiratory failure (n=3).Permanent discontinuation due to an adverse reaction occurred in 5% of patients who received Retevmo Adverse reactions resulting in permanent discontinuation in patients who received Retevmo included increased ALT (0.4%), sepsis (0.4%), increased AST (0.3%), drug hypersensitivity (0.3%), fatigue (0.3%), and thrombocytopenia (0.3%) • Dose interruptions due to an adverse reaction occurred in 42% of patients who received Retevmo. Adverse reactions requiring dosage interruption in ≥2% of patients included ALT increased, AST increased, hypertension, diarrhea, pyrexia, and QT prolongation • Dose reductions due to an adverse reaction occurred in 31% of patients who received Retevmo. Adverse reactions requiring dosage reductions in ≥2% of patients included ALT increased, AST increased, QT prolongation, and fatigue

*This does not reflect the full list of drug interactions. Please see full Prescribing Information for Retevmo.
CYP=cytochrome P450; ECG=electrocardiogram; H2=histamine H2 receptor.

Retevmo®
selpercatinib capsules
40 mg • 80 mg

IMPORTANT SAFETY INFORMATION FOR RETEVMO (CONTINUED)

Severe adverse reactions (Grade 3-4) occurring in ≥15% of patients who received Retevmo in LIBRETTO-001, were hypertension (18%), prolonged QT interval (4%), diarrhea (3.4%), dyspnea (2.3%), fatigue (2%), abdominal pain (1.9%), hemorrhage (1.9%), headache (1.4%), rash (0.7%), constipation (0.6%), nausea (0.6%), vomiting (0.3%), and edema (0.3%).

Serious adverse reactions occurred in 33% of patients who received Retevmo. The most frequently reported serious adverse reaction (in ≥ 2% of patients) was pneumonia.

Fatal adverse reactions occurred in 3% of patients; fatal adverse reactions which occurred in >1 patient included sepsis (n=3), cardiac arrest (n=3) and respiratory failure (n=3).

Common adverse reactions (all grades) occurring in ≥15% of patients who received Retevmo in LIBRETTO-001, were dry mouth (39%), diarrhea (37%), hypertension (35%), fatigue (35%), edema (35%), rash (27%), constipation (25%), nausea (23%), abdominal pain (23%), headache (23%), cough (18%), prolonged QT interval (17%), dyspnea (16%), vomiting (15%), and hemorrhage (15%).

Laboratory abnormalities (all grades; Grade 3-4) ≥20% worsening from baseline in patients who received Retevmo in LIBRETTO-001, were AST increased (51%; 8%), ALT increased (45%; 9%), increased glucose (44%; 2.2%), decreased leukocytes (43%; 1.6%), decreased albumin (42%; 0.7%), decreased calcium (41%; 3.8%), increased creatinine (37%; 1.0%), increased alkaline phosphatase (36%; 2.3%), decreased platelets (33%; 2.7%), increased total cholesterol (31%; 0.1%), decreased sodium (27%; 7%), decreased magnesium (24%; 0.6%), increased potassium (24%; 1.2%), increased bilirubin (23%; 2.0%), and decreased glucose (22%; 0.7%).

Concomitant use of **acid-reducing agents** decreases selpercatinib plasma concentrations which may reduce Retevmo anti-tumor activity. Avoid concomitant use of proton-pump inhibitors (PPIs), histamine-2 (H2) receptor antagonists, and locally-acting antacids with Retevmo. If coadministration cannot be avoided, take Retevmo with food (with a PPI) or modify its administration time (with a H2 receptor antagonist or a locally-acting antacid).

Concomitant use of **strong and moderate CYP3A inhibitors** increases selpercatinib plasma concentrations which may increase the risk of Retevmo adverse reactions including QTc interval prolongation. Avoid concomitant use of strong and moderate CYP3A inhibitors with Retevmo. If concomitant use of a strong or moderate CYP3A inhibitor cannot be avoided, reduce the Retevmo dosage as recommended and monitor the QT interval with ECGs more frequently.

Concomitant use of **strong and moderate CYP3A inducers** decreases selpercatinib plasma concentrations which may reduce Retevmo anti-tumor activity. Avoid coadministration of Retevmo with strong and moderate CYP3A inducers.

Concomitant use of Retevmo with **CYP2C8 and CYP3A substrates** increases their plasma concentrations which may increase the risk of adverse reactions related to these substrates. Avoid coadministration of Retevmo with CYP2C8 and CYP3A substrates where minimal concentration changes may lead to increased adverse reactions. If coadministration cannot be avoided, follow recommendations for CYP2C8 and CYP3A substrates provided in their approved product labeling.

The safety and effectiveness of Retevmo have not been established in **pediatric patients less than 12 years of age**. The safety and effectiveness of Retevmo have been established in pediatric patients aged 12 years and older for medullary thyroid cancer (MTC) who require systemic therapy and for advanced RET fusion-positive thyroid cancer who require systemic therapy and are radioactive iodine-refractory (if radioactive iodine is appropriate). Use of Retevmo for these indications is supported by evidence from adequate and well-controlled studies in adults with additional pharmacokinetic and safety data in pediatric patients aged 12 years and older. Monitor open growth plates in **adolescent patients.** Consider interrupting or discontinuing Retevmo if abnormalities occur.

No dosage modification is recommended for patients with **mild to severe renal impairment** (estimated Glomerular Filtration Rate [eGFR] ≥15 to 89 mL/min, estimated by Modification of Diet in Renal Disease [MDRD] equation). A recommended dosage has not been established for patients with end-stage renal disease.

Reduce the dose when administering Retevmo to patients with **severe hepatic impairment** (total bilirubin greater than 3 to 10 times upper limit of normal [ULN] and any AST). No dosage modification is recommended for patients with mild or moderate hepatic impairment. Monitor for Retevmo-related adverse reactions in patients with hepatic impairment.

Please see Important Safety Information throughout and click for full Prescribing Information for Retevmo.

SE HCP ISI All_25MAR2021

REFERENCES:

1. Retevmo (selpercatinib) [package insert]. Indianapolis, IN: Eli Lilly and Company; 2021.

2. Retevmo (selpercatinib) [safety data sheet]. Indianapolis, IN: Eli Lilly and Company; 2020.

Retevmo®
selpercatinib capsules
40 mg • 80 mg